# Complete Summary

## GUIDELINE TITLE

Clinical guideline for pharmacological management of type 2 diabetes.

## BIBLIOGRAPHIC SOURCE(S)

Joslin Diabetes Center. Clinical guideline for pharmacological management of type 2 diabetes. Boston (MA): Joslin Diabetes Center; 2007 Jan 12. 9 p. [91 references]

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline will be reviewed periodically and modified to reflect changes in clinical practice and available pharmacological information.

## ** REGULATORY ALERT **

## FDA WARNING/REGULATORY ALERT

**Note from the National Guideline Clearinghouse**: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- April 10, 2008, Exubera (insulin inhalation): Pfizer informed healthcare professionals and patients of updated safety information in the WARNINGS section of prescribing information for Exubera. This warning relates to a small number of primary lung malignancies that have been discovered in users of Exubera in clinical trials and post-marketing reports.
- February 26, 2008, Avandia (rosiglitazone): A new Medication Guide for Avandia must be provided with each prescription that is dispensed due to the U.S. Food and Drug Administration's (FDA's) determination that this medication could pose a serious and significant public health concern.
- November 14, 2007, Avandia (rosiglitazone): New information has been added to the existing boxed warning in Avandia's prescribing information about potential increased risk for heart attacks.
- October 16, 2007, Byetta (exenatide): Amylin Pharmaceuticals, Inc. has agreed to include information about acute pancreatitis in the PRECAUTIONS section of the product label.
- August 14, 2007, Thiazolidinedione class of antidiabetic drugs: Addition of a boxed warning to the updated label of the entire thiazolidinedione class of antidiabetic drugs to warn of the risks of heart failure.

## COMPLETE SUMMARY CONTENT



## SCOPE

### DISEASE/CONDITION(S)

Type 2 diabetes mellitus

### GUIDELINE CATEGORY

Diagnosis
Management
Treatment

### CLINICAL SPECIALTY

Endocrinology
Family Practice
Internal Medicine

### INTENDED USERS

Advanced Practice Nurses
Physician Assistants
Physicians

### GUIDELINE OBJECTIVE(S)

To support clinical practice and influence clinical behavior to improve outcomes and assure quality of care according to accepted standards for the pharmacological management of type 2 diabetes

### TARGET POPULATION

Non-pregnant adults with type 2 diabetes mellitus

### INTERVENTIONS AND PRACTICES CONSIDERED

1. Diagnosis
    - Casual plasma glucose
    - Fasting plasma glucose
    - Oral glucose tolerance test
2. Treatment
    - Glycemic control goals
    - Initial treatment
        - Mild presentation
        - Moderate presentation
        - Severe presentation
    - Oral antihyperglycemic therapy:
        - Metformin
        - Thiazolidinediones
        - Insulin secretagogue
        - Alpha–glucosidase inhibitor
        - Combination therapy
    - Insulin
        - Rapid-acting
        - Short-acting
        - Intermediate-acting
        - Long-acting
        - Pre-meal insulin mixture
    - Exenatide

### MAJOR OUTCOMES CONSIDERED

Glycemic control: fasting plasma glucose, 2-hour postprandial glucose, and bedtime glucose levels, percent hemoglobin

## METHODOLOGY

### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Review of all new papers on selected topics in PubMed, MEDLINE, OUID, Cochrane databases

### NUMBER OF SOURCE DOCUMENTS

Not stated

### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

| Grade of Recommendation | Clarity of Risk/Benefit | Quality of Supporting Evidence |
|---|---|---|
| **1A**<br><br>Strong recommendation<br>High quality of evidence | Benefits clearly outweigh risk and vice versa. | Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk. |
| **1B**<br><br>Strong recommendation<br>Moderate quality of evidence | Benefits clearly outweigh risk and burdens, or vice versa. | Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very strong evidence of some other research design. Further research is likely to have an impact on our confidence in the estimate of the benefit and risk and may change the estimate. |
| **1C**<br><br>Strong recommendation<br>Low quality of evidence | Benefits outweigh risk and burdens, or vice versa. | Evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws. Any estimate of effect is uncertain. |
| **2A**<br><br>Weak recommendation<br>High quality of evidence | Benefits closely balanced with risks and burdens. | Consistent evidence from well performed randomized, controlled trials or overwhelming evidence of some other form. Further research is unlikely to change our confidence in the estimate of benefit and risk. |
| **2B**<br><br>Weak recommendation<br>Moderate quality of evidence | Benefits closely balanced with risks and burdens; some uncertainty in the estimates of benefits, risks, | Evidence from randomized, controlled trials with important limitations (inconsistent results, methodological flaws, indirect or imprecise), or very |

| Grade of Recommendation | Clarity of Risk/Benefit | Quality of Supporting Evidence |
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| | and burdens. | strong evidence of some other research design. Further research is unlikely to have an impact on our confidence in the estimate of the benefit and risk and may change the estimate. |
| **2C**<br><br>Weak recommendation Low quality of evidence | Uncertainty in the estimates of benefits, risks, and burdens; benefits may be closely balanced with risks and burdens. | Evidence from observational studies, unsystematic clinical experience, or from randomized controlled trials with serious flaws. Any estimate of effect is uncertain. |

**METHODS USED TO ANALYZE THE EVIDENCE**

Review

**DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE**

Not stated

**METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Expert Consensus

**DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS**

Not stated

**RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS**

| Grade of Recommendation | Clarity of Risk/Benefit | Quality of Supporting Evidence |
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| **2C** | Uncertainty in the estimates of | Evidence from observational studies, |

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### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

### METHOD OF GUIDELINE VALIDATION

Peer Review

### DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The guideline was approved by the Joslin Clinical Oversight Committee on 1/12/07.

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

Definitions of the recommendation and evidence level grades (1A to 2C) are provided at the end of the "Major Recommendations" field.

| Diabetes Mellitus – Diagnostic Criteria (Non-Pregnant Adult) |
|---|
| • Casual plasma glucose $\geq$ 200 mg/dl and symptoms of diabetes (polyuria, polydipsia, ketoacidosis, or unexplained weight loss) **OR**<br>• Fasting plasma glucose (FPG) $\geq$ 126 mg/dl **OR**<br>• Results of a 2-hour 75-g Oral Glucose Tolerance Test (OGTT) $\geq$ 200 mg/dl |

| Goals of Glycemic Control for People with Diabetes[1] | | |
|---|---|---|
| **Biochemical Index** | **Normal** | **Goal** |
| Average Fasting Plasma Glucose or Preprandial Glucose (mg/dl) | < 100 | 90 – 130 |
| Average Postprandial 2 hours (mg/dl) | < 140 | < 160 |
| Average Bedtime Glucose (mg/dl) | < 120 | 110 – 150 |
| A1C (%) - sustained | < 6% | < 7%[2] |

[1]Laboratory methods measure plasma glucose. Most glucose monitors approved for home use calibrate whole blood glucose readings to plasma values. Plasma glucose values are 10-15% higher than whole

blood glucose values. It is important for people with diabetes to know whether their meters and strips record whole blood or plasma results.

[2]The true goal of care is to bring A1C as close to normal as safely possible. [**1C**] A goal of < 7% is chosen as a practical level for most patients using medications that may cause hypoglycemia to avoid the risk of that complication. Achieving normal blood glucose is recommended if it can be done practically and safely. **[1B]**

The guideline recommendations are presented in a series of algorithms on the following topics:

- Initial Treatment Strategy
- Considerations for Selecting Initial Oral Antihyperglycemic Therapy

Refer to the original guideline document for more information.

**Definitions**:

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| | | uncertain. |
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### CLINICAL ALGORITHM(S)

The original guideline document contains clinical algorithms for:

- Initial Treatment Strategy
- Considerations for Selecting Initial Oral Antihyperglycemic Therapy

## EVIDENCE SUPPORTING THE RECOMMENDATIONS

### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation.

## BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

### POTENTIAL BENEFITS

Appropriate pharmacological management of type 2 diabetes

### POTENTIAL HARMS

- Hypoglycemia
- Thiazolidinediones can be used in renal impairment but may increase fluid retention

## CONTRAINDICATIONS

### CONTRAINDICATIONS

- Metformin is contraindicated in the following conditions:
  - Creatinine $\geq$ 1.4 (women)
  - Creatinine $\geq$ 1.5 (men)
  - Intravenous (IV) contrast
  - Congestive heart failure (CHF)
  - Dehydration
  - Alcohol excess
  - $\geq$ 80 years of age (unless creatinine clearance is normal)
- Thiazolidinediones are contraindicated in the following conditions:
  - Class III or IV CHF
  - Liver function tests > 2.5 times upper limit of normal
- Insulin secretagogues (sulfonylurea or short-acting secretagogue) are contraindicated in the following conditions:
  - Sulfonylureas in severe liver or renal disease
- Alpha-glucosidase inhibitors are contraindicated in the following conditions:
  - Chronic intestinal disorders
  - Acarbose in cirrhosis
  - Acarbose and miglitol in renal impairment (creatinine > 2.0)
- Exenatide is contraindicated in gastroparesis requiring treatment with metoclopramide
- Inhaled insulin is contraindicated in smokers, recent smokers and patients with underlying lung disease

## QUALIFYING STATEMENTS

### QUALIFYING STATEMENTS

This Clinical Guideline is not intended to serve as a mandatory standard, but rather provides a set of recommendations for patient care management. These recommendations are not a substitute for sound and reasonable clinical judgment or decision-making and do not exclude other options. Clinical care must be individualized to the specific needs of each patient and interventions must be tailored accordingly. The guideline has been created to address initial presentation and treatment strategies in the adult non-pregnant patient population.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Living with Illness

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Joslin Diabetes Center. Clinical guideline for pharmacological management of type 2 diabetes. Boston (MA): Joslin Diabetes Center; 2007 Jan 12. 9 p. [91 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2007 Jan 12

### GUIDELINE DEVELOPER(S)

Joslin Diabetes Center - Hospital/Medical Center

### SOURCE(S) OF FUNDING

Joslin Diabetes Center

### GUIDELINE COMMITTEE

Joslin Clinical Oversight Committee

### COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

*Committee Members*: James Rosenzweig, MD (*Chairperson*); Richard Beaser, MD; Elizabeth Blair, MS, CS-ANP, CDE; Patty Bonsignore, MS, RN, CDE; Amy Campbell, MS, RD, CDE; Cathy Carver, ANP, CDE; Jerry Cavallerano, OD, PhD; Om Ganda, MD; John W. Hare, MD; Lori Laffel, MD, MPH; Melinda Maryniuk, MEd, RD; William Petit, MD; Kristi Silver, MD; Susan Sjostrom, JD; Kenneth Snow, MD; Robert Stanton, MD; William Sullivan, MD; Howard Wolpert, MD; Martin J. Abrahamson, MD (*ex officio*)

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## GUIDELINE STATUS

This is the current release of the guideline.

This guideline will be reviewed periodically and modified to reflect changes in clinical practice and available pharmacological information.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Joslin Diabetes Center.

Print copies: Available from the Joslin Diabetes Center, One Joslin Place, Boston, MA 02215

## AVAILABILITY OF COMPANION DOCUMENTS

None available

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI Institute on April 19, 2007. The information was verified by the guideline developer on May 10, 2007. This summary was updated by ECRI Institute on September 5, 2007 following the U.S. Food and Drug Administration advisory on the Thiazolidinedione class of antidiabetic drugs. This summary was updated by ECRI Institute on November 6, 2007, following the U.S. Food and Drug Administration advisory on Byetta (exenatide). This summary was updated by ECRI Institute on November 28, 2007 following the U.S. Food and Drug Administration advisory on the Avandia (rosiglitazone maleate) Tablets. This summary was updated by ECRI Institute on March 10, 2008 following the U.S. Food and Drug Administration advisory on Avandia (rosiglitazone maleate). This summary was updated by ECRI Institute on April 21, 2008 following the U.S. Food and Drug Administration advisory on Exubera (insulin human rDNA origin) Inhalation Powder.

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